



## RNA editing-dependent epitranscriptome diversity in cancer stem cells.

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development of a pan Bcl2 inhibitor for cancer stem cell directed therapy

## **Public Summary:**

Cancer stem cells (CSCs) can regenerate all facets of a tumour as a result of their stem cell-like capacity to self-renew, survive and become dormant in protective microenvironments. CSCs evolve during tumour progression in a manner that conforms to Charles Darwin's principle of natural selection. Although somatic DNA mutations and epigenetic alterations promote evolution, post-transcriptional RNA modifications together with RNA binding protein activity (the 'epitranscriptome') might also contribute to clonal evolution through dynamic determination of RNA function and gene expression diversity in response to environmental stimuli. Deregulation of these epitranscriptomic events contributes to CSC generation and maintenance, which governs cancer progression and drug resistance. In this Review, we discuss the role of malignant RNA processing in CSC generation and maintenance, including mechanisms of RNA methylation, RNA editing and RNA splicing, and the functional consequences of their aberrant regulation in human malignancies. Finally, we highlight the potential of these events as novel CSC biomarkers as well as therapeutic targets.

## **Scientific Abstract:**

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Deregulation of these epitranscriptomic events contributes to CSC generation and maintenance, which governs cancer progression and drug resistance. In this Review, we discuss the role of malignant RNA processing in CSC generation and maintenance, including mechanisms of RNA methylation, RNA editing and RNA splicing, and the functional consequences of their aberrant regulation in human malignancies. Finally, we highlight the potential of these events as novel CSC biomarkers as well as therapeutic targets.

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